

REMARKS/ARGUMENTS

Claims 15-17 and 23-24 are active.

Claim 15 has been amended to incorporate the previously presented limitations from Claim 22. Claim 22 has therefore been cancelled.

No new matter is added.

The claims of this application are directed to a method for the chromatographic analysis of total FSH (follicle stimulating) protein in which a poloxamer 188 surfactant is added to the protein solution during the analysis. According to the specification on pages 3 and 4 the addition of the poloxamer surfactant avoids protein loss and does not interfere with analysis in determining purity and concentration. The examples of this application provide a number of statistical analyses demonstrating that this is the case.

The rejection applied under 35 USC 103(a) combining Katakam and Wu cannot be sustained.

Applicants understand that Claim 22, which defined that the poloxamer is poloxamer 188, was included in the obviousness rejection. However, that position cannot be sustained.

In maintaining the rejection, the Examiner finds that “[a]t the time of the invention, it would have been obvious to one of the ordinary skill in the art to add Poloxamer to the FSH sample for size exclusion chromatography to improve yield, because Katakam teaches that Poloxamer polymer can stabilize protein against various processing stress.” (pages 2-3 of the Action).

First, the Examiner appears to have ignored the fact that Katakam does not describe FSH only HGH (human growth hormone). Indeed, there are no teachings in Katakam that allow one to envision the effects of Poloxamer surfactants on FSH. While it is true that Wu describes isolating FSH from bovine pituitary glands and Katakam discusses effects of HGH

aggregation in the presence of poloxamer, there are no teachings in this combination of art that even remotely suggests any problems with FSH.

HGH and FSH are very different proteins, have remarkably different structures and how one protein (HGH) acts in a given set of experiments (like in Katakam) provides no reasonable guidance as to how a second, distinct protein (FSH from Wu) would behave. HGH is a protein of about 200 amino acids and a molecular weight of 22 KD. The structure includes four helices for functional interaction with its receptor. In contrast, FSH is a **glycoprotein** composed of **two** polypeptide monomers, α and β .

The combination of Katakam and Wu do not provide any teachings as to how to assess total FSH protein in a chromatographic method as is defined in the claims.

Persons having ordinary skill in the art normally seek “to improve upon what is already generally known.” *In re Peterson*, 315 F.3d 1325, 1330 (Fed. Cir. 2003). However, before persons having ordinary skill in the art would want to optimize the choice or use of components in a claimed process, the prior art must at least generally recognize the process and generally suggest the components the claimed process utilizes to achieve its goals. To establish that Applicants’ claimed process would have been obvious to a person having ordinary skill in the art, the prior art must reasonably suggest that persons having ordinary skill in the art do what Applicants claims require. Here, the only suggestion to do what Applicants have done is Applicants’ own disclosure, i.e. hindsight.

Where, as here, the rejection of the subject matter Applicants claim is based on hindsight, the rejection is improper. *In re Fritch*, 972 F.2d at 1266; *In re Fine*, 837 F.2d at 1075.

Second, while the Examiner states that it would have been obvious to use any Poloxamer based on Katakam’s teachings, the Examiner ignores the fact that following the

teachings of Katakam, one would not have used Poloxamer 188 for size exclusion chromatography as alleged in the rejection. Table 1 (page 147) in Katakam clearly shows that Poloxamer 188 was the worst stabilizer amongst those tested. In fact, looking at the column corresponding to the critical micelle concentration (cmc) of each surfactant, it results that by using Poloxamer 188, a high level of protein aggregates were obtained (0.66) with very low soluble protein (0.03 mg/ml), which was the lowest of those surfactants tested.

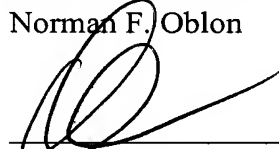
Conclusions of obviousness based on clearly erroneous findings, as is here the case, cannot stand. *Alza Corp. v. Mylan Labs., Inc.*, 464 F.3d 1286, 1289 (Fed. Cir. 2006).

Reconsideration and Withdrawal of the rejection is requested.

Allowance of this case is requested.

Respectfully submitted,

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